# Predicting the Effects of Changing PEEP Using a Basis Function Method

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Abstract: Current methods to optimise mechanical ventilation involve increasing positive end expiratory pressure (PEEP) in steps to maximize recruitment. If PEEP is too high, overdistension and damage occur. There is thus an inherent risk involved when increasing PEEP. This study predicts dynamic elastance and lung mechanics for higher PEEP using clinically relevant elastance basis functions, capturing distension, recruitment and constant stiffness, in a first order model of lung mechanics. The clinically relevant basis functions were used to fit elastance using a single compartment lung model for 10 patients undergoing recruitment maneuvers, where 2-4 PEEP levels were analysed, and then used to predict the elastance and pressure waveforms for PEEP level increases of 5 and 10 $\boldsymbol{cmH_2O}$. The mean error for the pressure fits from the clinically relevant basis functions was 2.06%. Mean error for pressure predictions with a PEEP level increase of 5 $\boldsymbol{cmH_2O}$ was 3.8-5.5%. Mean error for PEEP level increases of 10 $\boldsymbol{cmH_2O}$ was slightly higher, between 5.0 and 6.6%. Good pressure fits and predictions show these basis functions accurately fit and predict elastance and thus lung behavior at increased PEEP levels. Each clinically relevant basis function behaved as expected, however improvements to the identifiability of distension would further improve the overall accuracy.

*Keywords:* pressure, prediction, elastance, lung, recruitment, distension, airway

## 1. INTRODUCTION

Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) are common in the intensive care unit (ICU), and are associated with mortality up to 60% (Phua *et al.* 2009) and a substantial cost of care (Dasta *et al.* 2005). Mechanical ventilation (MV) supports the work of breathing and different MV modes can be tailored to individual patients via ventilator settings. However, there is no consensus best practice in selecting ventilation mode or settings (Sundaresan & Chase 2012). Equally, the way MV is implemented can strongly affect disease progression, outcome, and lung condition (Slutsky 1999). Therefore, it is important to optimise and tailor MV to the individual patient (Chiew *et al.* 2011).

Positive end-expiratory pressure (PEEP) is an important MV setting, which keeps alveoli open at end expiration and maintains recruitment (Gattinoni *et al.* 2010). PEEP selection and optimisation have been the focus of much research, with multiple attempts at creating a standardised "one size fits all" selection method (Brower *et al.* 2004). However, these methods do not account for the intra-patient variability and inter-patient heterogeneity. In clinical practice, PEEP selection thus relies heavily on intuition and experience, consensus guidelines, and/or cohort based outcomes (Kallet & Branson 2007). It thus requires a patient-specific "one method fits all" approach (Sundaresan & Chase 2012).

Model-based methods offer the ability to characterise patient-specific lung mechanics, and thus the potential to adapt MV care to individual patient condition. One such model-based measure of lung mechanics is elastance. Differing methods can identify an overall constant elastance ($E_{rs}$) for a breath, or a dynamic lung elastance ($E_{drs}$) that captures changes in elastance within a breath (Chiew *et al.* 2015a). One model-based method assesses elastance over various PEEP levels during a recruitment manoeuvre, and selects a new PEEP such that elastance is minimised (Chiew *et al.* 2011), matching recent clinical results (Amato *et al.* 2015).

One disadvantage of using recruitment manoeuvres to find a minimum elastance PEEP is it risks injury at non-optimum PEEP. In particular, high PEEP can cause overdistension of the lung, which can damage the lung and lead to worsened care (Parker, Hernandez & Peevy 1993). If model-based methods can be used to forward predict elastance at a moderately increased PEEP from the current level, PEEP selection for minimal elastance could be achieved with less risk.

In this study, basis functions are used to model the dynamic elastance ($E_{drs}$) of the lung within a breath. These basis functions relate elastance to physiologically and clinically relevant aspects of lung mechanics and condition, including recruitment and distension. The aim is to identify elastance basis functions in clinical data and evaluate their potential to capture and describe important aspects of patient MV. If successfully characterised, these individual aspects of the elastance may also add real-time clinical insight into patient lung condition and be useful in guiding patient-specific MV.

## 2. METHODS AND MATERIALS

### 2.1 Study Design

Data was obtained from a study of 10 patients diagnosed with ALI or ARDS ($PaO_2/FiO_2$ (PF ratio) between 150-300 mmHg) who underwent a recruitment manoeuvre (RM) (Sundaresan *et al.* 2011) in the Christchurch Hospital Intensive Care Unit (ICU), New Zealand. Table 1 gives the clinical details of the 10 patients recruited with their clinical diagnostics and PF ratios. Patients were ventilated using volume controlled (tidal

volume, $Vt \approx 400-600ml$ or $\approx 4-6\,mL/kg$) synchronised intermittent mandatory ventilation (SIMV) on Puritan Bennet PB840 ventilators (Covidien, Boulder, CO, USA). Spontaneous breathing efforts were prevented by sedation and muscle relaxants. This trial was approved by the New Zealand South Island Regional Ethics committee. Further details can be found in (Chiew *et al.* 2011).

Once steady state was reached, a single breath was analysed at each PEEP. Breath onset was defined as the point where flow went from negative to positive. Data was sampled at 100 Hz and the first and last 10% of each breath were discarded to ensure no unwanted inertial end effects from the ventilator (Chiew *et al.* 2015b). Computational analysis was performed using MATLAB (The Mathworks, Natick, MA, USA).

Table 1: Patient Demography (Chiew *et al.* 2011)

| Patients | Sex | Age (year) | Clinical Diagnostic | PF Ratio |
|---|---|---|---|---|
| 1 | F | 61 | Peritonitis, COPD | 214 |
| 2 | M | 22 | Trauma | 180 |
| 3 | M | 55 | Aspiration | 222 |
| 4 | M | 88 | Pneumonia, COPD | 165 |
| 5 | M | 59 | Pneumonia, COPD | 285 |
| 6 | M | 69 | Trauma | 280 |
| 7 | M | 56 | Legionnaires | 265 |
| 8 | F | 54 | Aspiration | 302 |
| 9 | M | 37 | H1N1, COPD* | 182 |
| 10 | M | 56 | Legionaires, COPD | 237 |
| *Chronic Obstructive Pulmonary Disease | | | | |

## 2.2 Model-based Analysis

### *2.2.1 Single Compartment Lung Model*

The basis functions in this study are fit in the same way as $E_{rs}$ and $E_{drs}$ are fit in (Chiew *et al.* 2011), using a single compartment lung model to fit the inspiration section of the breath. The single compartment lung model captures fundamental lung properties and mechanics in real time to identify either patient-specific constant lung elastance ($E_{rs}$) or time-varying, dynamic elastance ($E_{drs}$) during MV. The model uses measured airway pressure ($P_{aw}$), inspired volume ($V$), flow ($Q$) and PEEP with an integral based method (Hann *et al.* 2005). The model is derived in detail in (Chiew *et al.* 2011; Sundaresan *et al.* 2011), and is defined:

$$P_{aw}(t) = E_{rs}V(t) + R_{lung}Q(t) + PEEP \quad (1)$$

where $R_{lung}$ is the airway resistance. Using a pressure-varying dynamic elastance ($E_{drs}$) yields:

$$P_{aw}(t) = E_{drs}(P)\cdot V(t) + R_{lung}Q(t) + PEEP \quad (2)$$

### *2.2.2 Basis Function Definition*

$E_{drs}$ was broken up into clinically and physiologically relevant basis functions for: alveolar recruitment ($rec$); distension ($dist$); airway opening ($awo$); and a constant ($const$) for the chest wall and overall lung stiffness independent of condition. These functions were chosen to be continuous with pressure and to describe expected trends and/or effects in underlying lung mechanics as pressure changed during a volume controlled breath. A depiction of the four basis function shapes can be seen in Figure 1, along with key parameters.

The recruitment basis function was chosen as a decaying exponential with an offset allowing recruitment to begin at any point over inspiratory pressure, defined:

$$E_{rec}(P) = \begin{cases} a_{rec}e^{-b_{rec}P_{rec}} & if \quad P \le P_{rec} \\ a_{rec}e^{-b_{rec}P} & if \quad P > P_{rec} \end{cases} \quad (3)$$

Where the parameters characterising recruitment are the relative height of the function, $a_{rec}$, the starting pressure of the recruitment decay, $P_{rec}$ $P_{rec}$, and the decay exponent, $b_{rec}$ $b_{rec}$.

Distension was modelled as an increasing exponential that also had variable onset pressure, altering where it begins.

$$E_{dist}(P) = \begin{cases} 0 & if \quad P \le P_{dist} \\ a_{dist}(e^{b_{dist}P} - e^{b_{dist}P_{dist}}) & if \quad P > P_{dist} \end{cases} \quad (4)$$

Where $a_{dist}$ is the relative height of the function, $P_{dist}$ is the starting pressure for distension, and $b_{dist}$ is the decay exponent. If no distension exists a value of $a_{dist} = 0$ would be expected to be identified.

The third basis function is a linear decrease modelling sudden airway opening at the start of a breath, as seen in chronic obstructive pulmonary disease (COPD) or overly low PEEP levels below auto-PEEP (Chiew *et al.* 2011). This basis function has two parameters: a relative expansion/gradient $a_{awo}$, and an end point $P_{awo}$, and is defined:

$$E_{awo}(P) = \begin{cases} a_{awo}(P_{awo} - P) & if \quad P \le P_{awo} \\ 0 & if \quad P > P_{awo} \end{cases} \quad (5)$$

A fourth constant basis function, $E_{const}$ was used to describe the non-time varying part of the elastance, and captures a simple, constant lung compliance and the impact of static chest wall elastance.

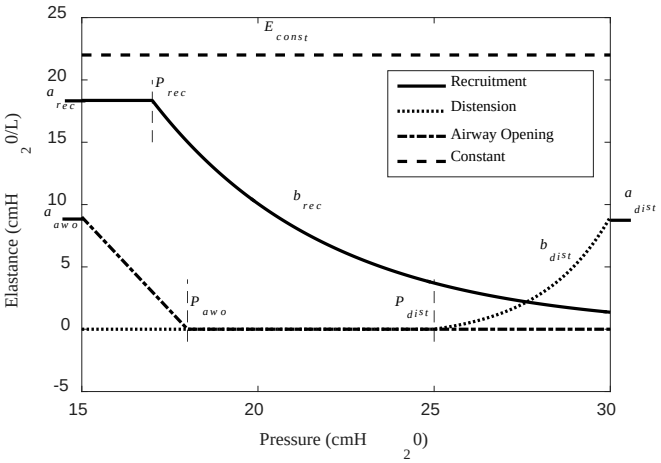


Figure 1: Schematic illustration of the four basis function shapes, showing the identified parameters of each function. Note: $a_{awo}$, $a_{rec}$ and $a_{dist}$ illustrate that the height of the shapes are relative to these parameters.

The four contributions of elastance are summed to define $E_{drs}$ over inspiratory pressure. Thus, (2) is modified to give:

$$P_{aw} = (E_{rec} + E_{dist} + E_{awo} + E_{const}) \cdot V + R \cdot Q + PEEP \quad (6)$$

Where:

$$E_{drs}(P) = E_{rec}(P) + E_{dist}(P) + E_{awo}(P) + E_{const} \quad (7)$$

Where functions of pressure over inspiration of a single volume controlled breath are also implicit functions of time, matching (Chiew *et al.* 2011) in overall approach.

Equations (3-5) are non-linear, and thus their parameters were fit using a grid search method, which iterated through a range of values for $(b_{dist}, b_{rec}, P_{rec}, P_{dist}, P_{awo})$. The range of iterated values for $b_{dist}$ and $b_{rec}$ were explicit values, whereas $P_{rec}, P_{dist}$, and $P_{awo}$ were found from a range of $P_{aw}$ values, where $n$ is the number of data points of $P_{aw}$, the ranges used for the grid search are defined:

$$\begin{gathered} b_{dist} = 0.2{:}\,0.3{:}\,2 \qquad b_{rec} = 0{:}\,0.05{:}\,0.2 \\ P_{rec} = P_{aw}(1{:}\,10{:}\,0.4 \times n) \qquad P_{dist} = P_{aw}(3{:}\,3{:}\,n) \\ P_{awo} = P_{aw}(1{:}\,10{:}\,0.6 \times n) \end{gathered} \quad (8)$$

For each grid search iteration the linear least squares integral method (Chiew *et al.* 2015b) was used to identify $a_{rec}, a_{dist}, a_{awo}$, and $E_{const}$ using (2-7). The parameters that created the lowest error determined the best-fit parameters, evaluated by mean absolute relative difference (MARD) between the modelled and measured pressure for each iteration of the grid search:

$$MARD = \frac{1}{n} \times \sum_{i=1}^{i=n} \frac{abs(P_{fit}^{i} - P_{aw}^{i})}{P_{aw}^{i}} \quad (9)$$

For this study, $R_{lung}$ is assumed to be a constant 5 $cmH_2Os/L$ (Chiew *et al.* 2011). However, when fitting pressure waveforms, if fitting error remained higher than a 10% difference between the model fit and the pressure data, the resistance was increased to 15 $cmH_2Os/L$ to account for patients which may have higher airway resistance, such as in COPD. Both values are clinically realistic (Chiew *et al.* 2011).

## 2.3 Forward Prediction

The summed basis function elastance (7) is plotted against pressure. Initial observations indicated a decreasing exponential curve could be fit through the mean $E_{drs}$, or $E_{rs}$ value, which could potentially be used to predict a trend in the elastance behaviour over pressure outside the current breath. Physically, the decreasing exponential could imply greater pulmonary recruitment and therefore lower elastance at higher PEEP. Hence, an exponential curve was fit to this data and used to predict initial elastance at a higher PEEP.

To model the increase in elastance that occurs due to overdistension at higher pressures and PEEP, the clinically relevant distension basis function was used to determine the onset of distension. The first PEEP to show significant distension, defined by $\max(E_{dist}) > 0.1\ cmH_2O/L$, was used to define the onset of distension, and a linear relationship was formulated with the start point of the mean of the first $E_{drs}$ to show distension and a gradient equal to the size parameter of the relevant distension function basis function ($a_{dist}$). This approach allows distension to be included in predictions along with recruitment, as PEEP rises and some distension increases in likelihood.

First, $E_{drs}$ was fit using (3-7) to breaths at lower PEEP values ($PEEP_{n-2}$, $PEEP_{n-1}$, $PEEP_n$). The decreasing exponential trend was then fit through the three mean $E_{drs}$ values. This exponential trend line was then used to extrapolate for the mean $E_{drs}$ at a higher PEEP ($E_{n+1}$). The ratio of the new mean $E_{drs}$ to the highest mean $E_{drs}$ of the predicting breath ($E_n$) was then calculated:

$$Ratio = E_{n+1} / E_n \quad (10)$$

The $E_{drs}$ of the $PEEP_n$ predicting breath ($E_{drs\_n}$) was then multiplied by $Ratio$ to estimate $E_{drs}$ of the new breath ($E_{drs\_n+1}$). This predicted $E_{drs\_n+1}$, could then be used to simulate the pressure waveform using (6). Since, in clinical applications, the volume and flow waveforms of sedated patients tend to be consistent breath to breath, the volume and flow at $PEEP_n$ was used to simulate Equation (2) and obtain predicted pressure at $PEEP_{n+1}$.

As well as simply using the first 3 prior PEEP levels ($PEEP_{n-2}$, $PEEP_{n-1}$, $PEEP_n$) to predict the next PEEP level ($PEEP_{n+1}$), forward prediction was tested with different predicting and predicted PEEP levels to determine the impact of the proximity to the predicted results and the impact of using more or less data points on the prediction accuracy. Using the data available, the predictions tested are shown in Table 2. Thus, predictions were made with 2-4 prior PEEP levels to estimate pressure and distension at a $PEEP_{n+1}$ 5 $cmH_2O$ higher.

Table 2: Description of the predictions with the number of input PEEP levels, the PEEP increase for prediction and the PEEP levels that were predicted.

| Prior Number of PEEP Levels | ΔPEEP Predicted ($cmH_2O$) | Predicted PEEP levels ($cmH_2O$) |
|---|---|---|
| 2 | 5 | 15,20,25 |
| 2 | 10 | 20,25 |
| 3 | 5 | 20,25 |
| 3 | 10 | 25 |
| 4 | 5 | 25 |

# 3. RESULTS

## 3.1 Basis Function Fit

Figure 2 shows examples of the modelled vs measured pressure for Patients 2, 4, 5 and 6. Table 3 gives the MARD for the pressure fit between the modelled and measured pressure for all patients. The mean MARD between modelled and measured pressure across all patient breaths was 2.06%, indicating the basis functions accurately captured observed pressure dynamics. Notably, Patient 5, did not fit the model well for a PEEP = 5 $cmH_2O$, with a MARD of 27.50%, as seen in Figure 2, which may have been due to Auto-PEEP of 8 $cmH_2O$ (Sundaresan *et al.* 2011).

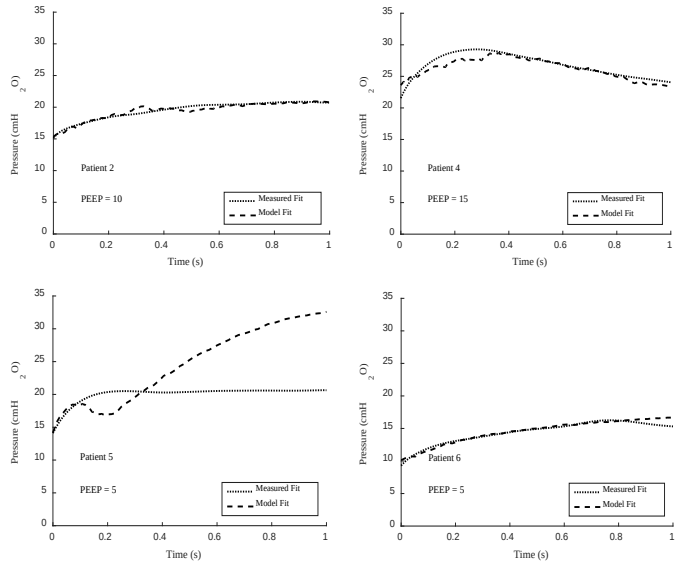


Figure 2: Basis function modelled pressure fits compared with measured pressure for patients 2,4,5 and 6. Patient 4 had an increase resistance of 5 $cmH_2O/L$ . Patient 5 could not be modelled accurately at a PEEP of 5, and is a worst case, where others shown are typical of the MARD of 2.06 %.

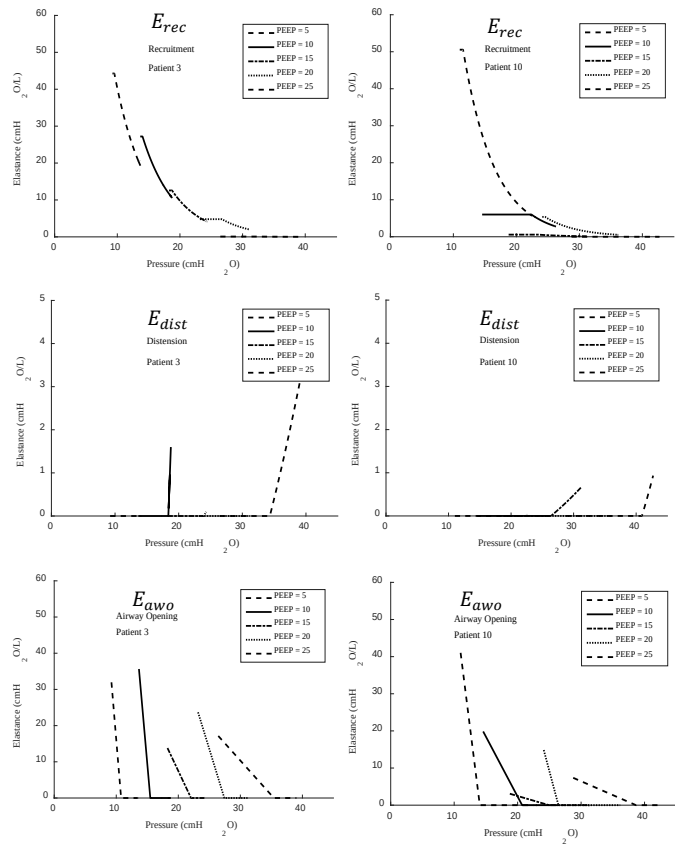


Figure 3: Depiction of $E_{rec}$, $E_{dist}$ and $E_{awo}$ for all breaths of Patient 3 and 10.

To validate if the basis functions characterise underlying lung mechanics, $E_{rec}$, $E_{dist}$ and $E_{awo}$ are first plotted over a range of breaths for Patients 3 and 10 in Figure 3.

## 3.2 Forward Prediction Results

Figure 4 shows $E_{drs}$ derived using identified basis functions across several PEEP levels for Patients 2, 6, 8, and 10, as well as mean $E_{drs}$ and the exponential trend fit to the mean $E_{drs}$ of the first 3 PEEP levels. The decreasing exponential trend indicates these 4 patients undergo recruitment across these first 3 PEEP levels. Patients 2, 10 had max $E_{dist} > 0.1 cmH_2O/L$ at PEEP = 15 $cmH_2O$. Therefore, a linear increase representing distension was included in the prediction curve, yielding the upward prediction curves in Patients 2 and 10.

Table 4 gives the MARD for the pressure fit from the predicted $E_{drs}$ of the patients. Patient 7 had data for a PEEP of 16 $cmH_2O$ instead of 20 $cmH_2O$ and no higher PEEP breaths. Therefore, the forward prediction of this patient was omitted. Patient 9 was also omitted due to not having measured breaths at PEEP of 5 or 10 $cmH_2O$, which were not done for clinical reasons (Chiew *et al.* 2011).

The mean MARD between predicted and measured pressure using input PEEP of 5, 10 and 15 $cmH_2O$ was found to be 4.1% and 6.6% for predicting PEEP of 20 and 25 $cmH_2O$ respectively. The mean MARD for predicting the pressure for PEEP of 25 $cmH_2O$ was 4.4% when using input PEEP of 15 and 20, and also 4.4% when using input data from PEEP of 10, 15 and 20 $cmH_2O$, and 5.5% when using data from input PEEP of 5,10, 15 and 20 $cmH_2O$. The large error of 6.6 % when predicting PEEP of 25 $cmH_2O$ from input PEEP of 5,10 and 15 $cmH_2O$, a forward prediction of 10 $cmH_2O$, reflects the expected trend that forward prediction of PEEP is reasonably accurate for smaller increases in PEEP, but as the change in PEEP increases, error increases. This effect was also prevalent when predicting the PEEP of 20 $cmH_2O$, the mean MARD for this case with training PEEP of 5 and 10 $cmH_2O$ was 5.0%, and was 4.3% for the closer input PEEP of 10 and 15 $cmH_2O$.

For these results Figure 5 shows good pressure prediction for various PEEP change predictions for Patients 2, 4, 8 and 10 who displayed notable recruitment behaviour (Chiew *et al.* 2011). Notably Patient 2 at PEEP = 22 has significant distension, as seen in Figure 5. However, this effect is captured well and the predicted pressure matches well.

Table 3: MARD between modelled basis function pressure and measured pressure for all 10 patients

| Patients | Pressure Fit Error from basis functions (%) | | | | |
|---|---|---|---|---|---|
| | PEEP ($cmH_2O$) | | | | |
| | 5 | 10 | 15 | 20 | 25 |
| 1 | 7.21 | 2.55 | 2.04 | 1.77 | 0.89 |
| 2 | 1.78 | 1.44 | 0.61 | 0.76 | 1.22*** |
| 3 | 1.95 | 1.00 | 0.59 | 0.57 | 0.57 |
| 4* | 4.84 | 3.21 | 2.44 | 1.74 | 1.81 |
| 5 | 27.08 | 3.02 | 2.64 | 0.93 | 0.56 |
| 6 | 2.02 | 2.16 | 0.96 | 0.95 | 1.02 |
| 7 | 1.01 | 0.89 | 1.29 | 0.49** | N/A |
| 8 | 3.59 | 2.13 | 1.29 | 1.14 | 1.91 |
| 9 | 1.21 | 1.07 | 0.89 | 0.54 | 0.50 |
| 10 | 1.08 | 0.59 | 0.36 | 0.49 | 0.24 |
| Mean error | 2.06 | | | | |

* $R_{lung} = 15\ cmH_2O$ instead of 5 $cmH_2O$ to improve fit
* * PEEP of 16 recorded instead of PEEP=20, no PEEP=25 breath
***PEEP of 22 recorded instead of PEEP=25

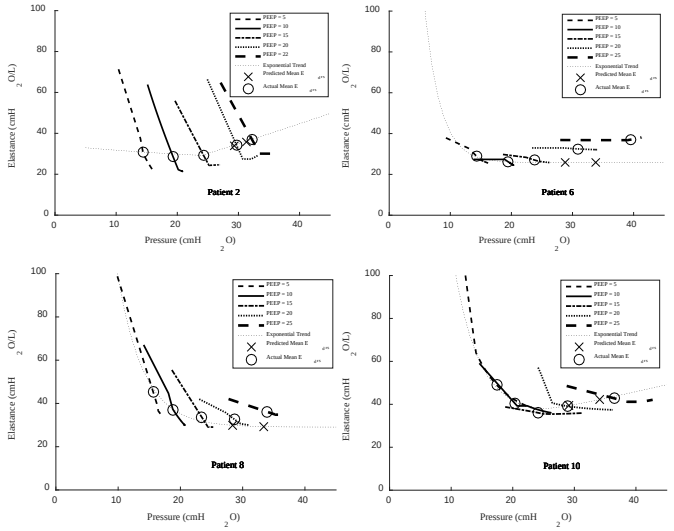


Figure 4: Dynamic Elastance from basis function plots with the exponential trend through mean $E_{drs}$. Also shown are the predicted mean $E_{drs}$.

Table 4: Pressure fit error between the predicted pressure fit and the measured pressure for all 8 patients that could be fitt with recruitment

| | | Predicted Pressure fit error (%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Input PEEP ($cmH_2O$) | | 5, 10 | 10, 15 | 5, 10, 15 | 15, 20 | 10, 15, 20 | 5,10, 15, 20 | 5, 10 | 10, 15 | 5, 10, 15 |
| Predicted PEEP ($cmH_2O$) | | 15 | 20 | 20 | 25 | 25 | 25 | 20 | 25 | 25 |
| Patients | 1 | 4.9 | 8.0 | 6.7 | 5.0 | 3.5 | 10.2 | 10.2 | 9.0 | 9.6 |
| | 2** | 2.0 | 0.4 | 1.8 | 0.6 | 1.2 | 0.9 | 2.6 | 1.1 | 1.1 |
| | 3 | 3.1 | 4.5 | 2.4 | 1.6 | 1.4 | 1.3 | 5.1 | 2.5 | 2.2 |
| | 4* | 3.1 | 5.9 | 4.1 | 7.9 | 8.4 | 9.1 | 6.5 | 7.5 | 8.3 |
| | 5 | 4.0 | 2.5 | 4.1 | 7.5 | 7.5 | 6.8 | 2.8 | 11.5 | 11.5 |
| | 6 | 9.8 | 3.2 | 5.1 | 5.0 | 5.2 | 6.6 | 2.5 | 7.6 | 8.4 |
| | 8 | 1.9 | 7.4 | 6.1 | 6.1 | 6.4 | 6.7 | 7.3 | 7.4 | 7.9 |
| | 10 | 1.6 | 2.2 | 2.6 | 1.4 | 1.6 | 2.6 | 2.9 | 3.4 | 3.7 |
| Mean error | | 3.8 | 4.3 | 4.1 | 4.4 | 4.4 | 5.5 | 5.0 | 6.2 | 6.6 |

* Airway resistance of 15 $cmH_2O$ instead of 5 $cmH_2O$ to improve fit
**Predicted PEEP recorded was 22 instead of 25 $cmH_2O$

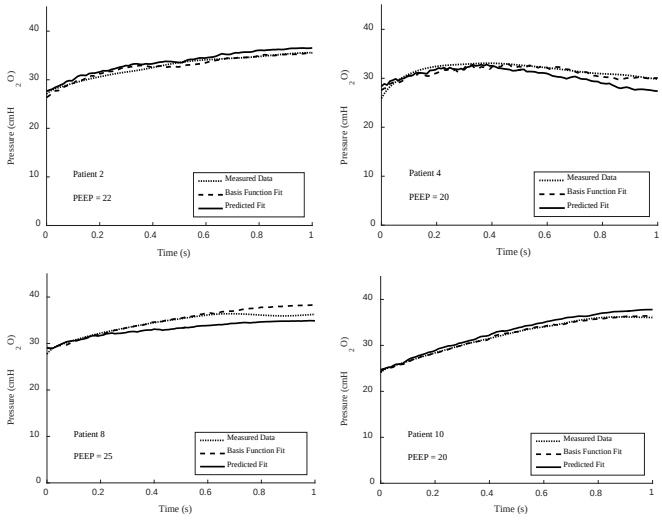


Figure 5: Examples of predicted waveforms compared to pressure data and basis function model fits. All plots are with training PEEP of 5, 10 and 15.

# 4. DISCUSSION

## 4.1 Clinically Relevant Basis Functions

The mean error for pressure fitting basis function $E_{drs}$ to data was 2.06%, showing clinically relevant basis functions can capture clinically measured pressure dynamics in MV patients. While it is difficult to validate the accuracy of the underlying basis functions, the accurate model fit and predictive power suggests they successfully characterise underlying lung mechanics. Figure 3 shows $E_{rec}$ decreases as PEEP increases, as expected since higher PEEP maintains greater recruitment at end of expiration, reducing in-breath recruitment. The overall decrease in elastance occurs due to the lung becoming more compliant as more alveoli are opened and thus, recruited, matching the observed results (Chiew *et al.* 2011).

Equally, distension is expected to increase as PEEP increases, due to higher pressures overinflating the lung. Figure 3 shows this effect, for $E_{dist}$ in Patient 3. However, some PEEP breaths, such as at PEEP of 20 $cmH_2O$, Patients 3 and 10 do not register any identified distension, which is also clinically possible. In particular distension may occur at different levels for each patient and is not as predictable as increased recruitment as PEEP rises. Further research should be done to validate the relevance of each basis function shape.

Patient 4 needed higher airway resistance for an accurate fit, most likely due to the fact the patient is very elderly, and may have more resistive and constricted airways, limiting airflow and increasing resistance (Lalley 2013). A typical resistance of 5 $cmH_20s/L$ could induce inaccuracies in all patients in identifying basis function parameters. However, the forward predictions would not be strongly affected, as all dynamic elastances of a patient would be shifted by a relatively similar amount with the consistent flow rates used across PEEP steps in the clinical data used in this analysis. To better validate the clinical aspects of the basis functions, the constant resistance may need to be identified and become patient specific as in (Langdon *et al.* 2016).

## 4.2 Forward Prediction

Forward predictions in were found to be accurate with an average MARD of 3.79-5.53% for all predictions with a PEEP increase of 5 $cmH_2O$ which is relatively large compared to more typical steps of 2-3 $cmH_2O$ (Langdon *et al.* 2016). A MARD of 6.58% was observed when predicting pressure responses to a PEEP of 25 $cmH_2O$ from input PEEP 5, 10, 15 $cmH_2O$. MARD was 6.23% for predicting a pressures at a PEEP of 25 $cmH_2O$ from input data at a PEEP of 10, 15, and 4.97% for predicting pressures at a PEEP of 20 from input PEEP 5, 10. These prediction results provide a promising starting point for forward prediction of elastance, and thus evaluating lung mechanics and MV safety with different PEEP before clinical application. In particular, forward prediction of increasing PEEP can prevent overdistension and iatrogenic damage. Thus, this approach can allow PEEP to be safely varied in a patient-specific manner, improving MV delivery and thus patient outcomes.

Including extra data points did not significantly affect the model's ability to predict pressure across high PEEP level changes, with a 4.11% mean MARD for 3 input PEEP levels and 4.26% for 2 input PEEP levels when predicting PEEP =20. In fact, it worsened accuracy very slightly in one case, with 5.53% mean MARD for 4 data points and 4.40% for 2 and 3 data points when predicting PEEP =25. This outcome may be due to the intrinsic need to make assumptions when modelling physiological characteristics like distension. Equally, the trend may not be an exact exponential, and thus the short term trend given by the closest PEEP is more accurate at predicting the next elastance.

### 4.3 Limitations

The basis functions did not fit all patient dynamics at all PEEP levels consistently. Patient 5 at PEEP = 5 $cmH_2O$ (Figure 2) had an increase in pressure at the start of the breath that was too steep for the model dynamics to fit. The lack of model fit resulted in a MARD of 27.50%. Thus, these basis functions may not be applicable for all patients and/or PEEP levels. Equally, it may have been an outlying case at a particularly low PEEP = 5 $cmH_2O$ that is not typically clinically used.

Figure 4 shows a limitation in attempting to fit the onset and amount of distension as PEEP increases, with distension modelled by a linear line from an onset pressure point. For Patients 2 and 10, this linear increase works well and predicts the high PEEP breaths accurately. However, Patients 6 and 8 do not show distension from $E_{dist}$, even though $E_{drs}$ increases as PEEP increases. This behaviour indicates the forward prediction method is not as accurate for every patient due to inter-patient variability and possible limitations in the chosen $E_{dist}$ basis function not capturing distension as it is seen in the patient data. Equally, these patients may simply not have displayed enough distension for the basis function defined to capture.

## 5. CONCLUSIONS

This paper presents a set of physiologically relevant basis functions used to identify patient and breath specific lung mechanics in a clinically validated model. The relevance of the basis functions allows additional insight into distension and recruitment to be obtained. The use of data from two or more PEEP levels in a recruitment maneuver can be used to accurately predict elastance, and thus pressure and distension at a higher PEEP level, thus reducing risk and increasing patient safety. The approach is generalisable, and provides an initial potential method for further clinical validation.

## REFERENCES


Amato, M.B.,Meade, M.O.,Slutsky, A.S.,Brochard, L.,Costa, E.L.,Schoenfeld, D.A.,Stewart, T.E.,Briel, M.,Talmor, D. & Mercat, A. 2015, 'Driving pressure and survival in the acute respiratory distress syndrome', *New England Journal of Medicine*, vol. 372, no. 8, pp. 747-755.

Brower, R.,Lanken, P.,MacIntyre, N.,Matthay, M.,Morris, A.,Ancukiewicz, M.,Schoenfeld, D. & Thompson, B. 2004, 'Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome', *The New England journal of medicine*, vol. 351, no. 4, pp. 327-336.

Chiew, Y.S.,Chase, J.G.,Shaw, G.,Sundaresan, A. & Desaive, T. 2011, 'Model-based PEEP optimisation in mechanical ventilation', *Biomedical engineering online*, vol. 10, no. 1, p. 111.

Chiew, Y.S.,Pretty, C.,Docherty, P.D.,Lambermont, B.,Shaw, G.M.,Desaive, T. & Chase, J.G. 2015a, 'Time-varying respiratory system elastance: a physiological model for patients who are spontaneously breathing', *PloS one*, vol. 10, no. 1, p. e0114847.

Chiew, Y.S.,Pretty, C.G.,Shaw, G.M.,Chiew, Y.W.,Lambermont, B.,Desaive, T. & Chase, J.G. 2015b, 'Feasibility of titrating PEEP to minimum elastance for mechanically ventilated patients', *Pilot and Feasibility Studies*, vol. 1, no. 1, p. 1.

Dasta, J.F.,McLaughlin, T.P.,Mody, S.H. & Piech, C.T. 2005, 'Daily cost of an intensive care unit day: the contribution of mechanical ventilation', *Critical care medicine*, vol. 33, no. 6, pp. 1266-1271.

Gattinoni, L.,Carlesso, E.,Brazzi, L. & Caironi, P. 2010, 'Positive end-expiratory pressure', *Current opinion in critical care*, vol. 16, no. 1, pp. 39-44.

Hann, C.E.,Chase, J.G.,Lin, J.,Lotz, T.,Doran, C.V. & Shaw, G.M. 2005, 'Integral-based parameter identification for long-term dynamic verification of a glucose–insulin system model', *Computer methods and programs in biomedicine*, vol. 77, no. 3, pp. 259-270.

Kallet, R.H. & Branson, R.D. 2007, 'Do the NIH ARDS clinical trials network PEEP/FIO2 tables provide the best evidence-based guide to balancing PEEP and FIO2 settings in adults?', *Respiratory Care*, vol. 52, no. 4, pp. 461-477.

Lalley, P.M. 2013, 'The aging respiratory system—pulmonary structure, function and neural control', *Respiratory physiology & neurobiology*, vol. 187, no. 3, pp. 199-210.

Langdon, R.,Docherty, P.D.,Chiew, Y.S. & Chase, J.G. 2016, 'Extrapolation of a non-linear autoregressive model of pulmonary mechanics', *Mathematical Biosciences*.

Parker, J.C.,Hernandez, L.A. & Peevy, K.J. 1993, 'Mechanisms of ventilator-induced lung injury', *Critical care medicine*, vol. 21, no. 1, pp. 131-143.

Phua, J.,Badia, J.R.,Adhikari, N.K.,Friedrich, J.O.,Fowler, R.A.,Singh, J.M.,Scales, D.C.,Stather, D.R.,Li, A. & Jones, A. 2009, 'Has mortality from acute respiratory distress syndrome decreased over time? A systematic review', *American journal of respiratory and critical care medicine*, vol. 179, no. 3, pp. 220-227.

Slutsky, A.S. 1999, 'Lung injury caused by mechanical ventilation', *CHEST Journal*, vol. 116, no. suppl_1, pp. 9S-15S.

Sundaresan, A. & Chase, J.G. 2012, 'Positive end expiratory pressure in patients with acute respiratory distress syndrome–The past, present and future', *Biomedical Signal Processing and Control*, vol. 7, no. 2, pp. 93-103.

Sundaresan, A.,Chase, J.G.,Shaw, G.,Chiew, Y.S. & Desaive, T. 2011, 'Model-based optimal PEEP in mechanically ventilated ARDS patients in the Intensive Care Unit', *BioMedical Engineering OnLine*, vol. 10, no. 1, p. 64.